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EXAMINER	
SHEIKH, HUMERA N	

ART UNIT	PAPER NUMBER
1615	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/518,035	ROYER, GARFIELD P.	
	Examiner	Art Unit	
	Humera N. Sheikh	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 March 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-41* is/are pending in the application.

4a) Of the above claim(s) *5,11-14,17,20-26,28-34,36-38 and 41* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4, 6-10, 15, 16, 18, 19, 27, 35, 39 and 40* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of the Application

Receipt of the Response after Non-Final Office Action, the Amendment and Applicant's Arguments/Remarks, all filed 03/13/09 is acknowledged.

Applicant has overcome the following rejections by virtue of the amendment and/or persuasive remarks: (1) The 35 U.S.C. §112, second paragraph rejection of claim 16 has been withdrawn; and (2) The 35 U.S.C. §103(a) rejection over Petersen (US 2002/0071827 A1) in view of Bell (US 2002/0055143 A1) has been withdrawn.

Claims 1-4, 6-10, 15, 16, 18, 19, 27, 35, 39 and 40 have been examined in this action. Claim 16 has been amended. Claims 42-44 have been cancelled. Claims 5, 11-14, 17, 20-26, 28-34, 36-38 and 41 have been withdrawn (non-elected invention). Claims 1-4, 6-10, 15, 16, 18, 19, 27, 35, 39 and 40 remain rejected.

Claim Rejections - 35 USC § 103

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 1-4, 6-10, 15, 16, 19, 27, 35, 39 and 40 are rejected under 35 U.S.C. 103(a) as being unpatentable over Saito *et al.* (hereinafter "Saito") (U.S. Patent No. 6,344,209) in view of Bell *et al.* (hereinafter "Bell") (U.S. Pat. Appln. Publn. No. 2002/0055143 A1).

Saito ('209) teaches an apatite-coated solid composition containing a biodegradable polymer, an apatite-coated solid composition containing a biodegradable polymer and a

medicinal substance having sustained release properties and a method for producing the solid composition (see column 1, lines 6-10); (col. 2, line 39 – col. 3, line 37) and Abstract.

Suitable biodegradable polymers disclosed include hyaluronates, polyethylene glycol and gelatin, for example (col. 4, lines 43-64).

Suitable medicinal substances disclosed are anti–tumor agents including antineoplastic agents such as cisplatin (col. 6, line 65 – col. 7, line 3). The medicinal substance is employed before molding with the aid of suitable excipients such as calcium sulfate hemihydrate (col. 15, lines 21-33).

The pharmaceutical composition can be produced by dissolving a biodegradable polymer in which the medicinal substance is dispersed and forming the solution into spheres, rods, needles, pellets, films or the like by an appropriate method (col. 17, lines 59-67).

In accordance with the invention, a substrate, i.e., (1) a solid composition containing a biodegradable polymer, (2) a solid composition containing a biodegradable polymer and a medicinal substance is immersed in an apatite-forming buffer solution so as to coat the surface of the substrate with apatite. The substrate is preferably used in granular form (granules, fine particles, fine granules) (col. 15, lines 8-20); (col. 16, lines 1-9). Also see column 3, lines 18-37), whereby Saito teaches a method for producing the solid composition comprising a biodegradable polymer and medicinal agent.

The apatite-coated solid composition can be processed into an injectable product by suspending the composition together with a dispersant, using for example, polysaccharides such as hyaluronic acid (col. 20, lines 9-32).

Acids such as aspartic acid and glutamic acid are disclosed at column 14, lines 64-65. This teaching meets the limitation of a 'complexing agent' as in instant claim 10.

Saito teaches that the apatite-coated solid composition can be used directly or used as a material for the manufacture of various dosage forms. Parenteral dosage forms can be administered topically (e.g., subcutaneous injections, implants, etc.) (col. 19, line 66 - col. 20, line 8).

The apatite-coated solid composition can be used to treat and repair bone tissue after surgery for lung cancer, breast cancer, etc. (col. 20, lines 43-58).

The examples at columns 22-24 demonstrate processes for preparing the apatite-coated solid compositions which contain biodegradable polymers.

Saito does not teach the matrix polymer - dextran sulfate.

Bell ('143) teaches bone precursor compositions suitable for injection, which contain glucosaminoglycans and polysaccharides, including dextran sulfate, chondroitin sulfate and hyaluronic acid (see ¶s [0072-0073]) as well as inorganic compounds such as calcium sulfate hemihydrate, therapeutic agents and colony stimulating factors (CSF). The glucosaminoglycans and polysaccharides (i.e., dextran sulfate) are useful in the development or regeneration of tissue structure and function (¶ [0068]).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to incorporate the glucosaminoglycans and polysaccharides (i.e., dextran sulfate of Bell within the coated solid compositions of Saito. One would do so with a reasonable expectation of success because Bell teaches bone precursor compositions that comprise

polysaccharides, such as dextran sulfate, which contain biological, physiological and structural information for the development or regeneration of tissue structure and function. The expected result would be an improved composition for treating diseases and conditions of bone.

* * * * *

Claim 18 is rejected under 35 U.S.C. 103(a) as being unpatentable over Saito *et al.* (hereinafter "Saito") (U.S. Patent No. 6,344,209) in view of Bell *et al.* (hereinafter "Bell") (U.S. Pat. Appln. Publn. No. 2002/0055143 A1) as applied to claims 1-4, 6-10, 15, 16, 19, 27, 35, 39 and 40 above and further in view of Petersen *et al.* (hereinafter "Petersen") (U.S. Pat. Appln. Publn. No. 2002/0071827 A1).

The teachings of Saito are discussed above. Saito does not teach hydroxypropylmethyl cellulose (HPMC).

Petersen ('827) teaches a bone graft substitute composition that may include a mixture comprising calcium sulfate hemihydrate, plasticizing substances - cellulose derivatives such as hydroxypropylmethyl cellulose, bioactive agents such as hyaluronic acid, growth factors, bone marrow, etc. and additives such as antitumor agents. See ¶s [0014]-[0020]; [0041]-[0045]. The bone graft substitute composition can be mixed into a paste and then loaded into a syringe and ejected for an extended period of time [0016].

It would have been obvious to one of ordinary skill in the art at the time the invention was made to incorporate the HPMC of Petersen within the apatite-coated solid composition of Saito. One would do so with a reasonable expectation of success because Petersen teaches inclusion of cellulose derivatives (i.e., HPMC) as an effective means to provide beneficial effects

and properties, such as plasticizing properties. The expected result would be an enhanced composition for the treatment of diseases, such as cancer.

* * * * *

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

(1) Claims 1-4, 9, 10, 16, 19, 27 and 35 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-3, 13, 15-19 and 29 of U.S. Patent No. 6,391,336 ('336 Patent). Although the conflicting claims are not identical, they are not patentably distinct from each other because the '336 Patent also claims a solid composition comprising an aqueous mixture of: a) an antineoplastic agent, b) a calcium sulfate

hemihydrate and a complexing agent, whereby the composition is based on the hydration reaction product of the aqueous mixture.

(2) Claims 1-4, 6-10, 16, 19, 27 and 35 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 3-7, 12-14, 16-17, 20, 28, 44-45 and 48-49 of U.S. Patent No. 6,497,901 ('901 Patent). Although the conflicting claims are not identical, they are not patentably distinct from each other because the '901 Patent also claims a matrix delivery system comprising a) calcium sulfate, b) a conditioning agent, c) a matrix polymer, d) a complexing agent and e) an antineoplastic agent, whereby the matrix delivery system becomes a solid by hydration.

(3) Claims 39 and 40 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-6, 17, 18, 33 and 35-39 of U.S. Patent No. 6,630,486 ('486 Patent). Although the conflicting claims are not identical, they are not patentably distinct from each other because the '486 Patent also claims a method of producing sustained release of an active agent comprising administering a solid composition comprised of a) an active agent, b) calcium sulfate hemihydrate, c) a matrix polymer and/or d) a complexing agent, whereby the composition is in the form that includes a bead, tablet, wafer, sphere, granule or cylinder.

(4) Claims 1-4, 6-8, 16, 19 and 27 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 73, 74 and 76-

80 of copending Application No. 10/838,303 ('303 application). Although the conflicting claims are not identical, they are not patentably distinct from each other because the '303 application also claims a solid composition for the controlled release of an active agent comprising a) calcium sulfatel, b) a conditioning agent (calcium stearate) and a matrix polymer whereby the composition is a solid matrix due to the hydration of the calcium sulfate.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

* * * * *

Response to Arguments

Applicant's arguments filed 03/13/09 have been fully considered and were found to be partially persuasive.

- **Rejection under 35 U.S.C. §112, second paragraph:**

Applicant argued, "The parenthetical expression has been eliminated from claim 16 so as to obviate this rejection."

Applicant's arguments were persuasive based on the amendment to claim 16, which removes, "(>100,000 MW)" from the claim limitation.

- **Rejection under 35 U.S.C. §103(a) over Saito (USPN 6,344,209) & Bell (US 2002/0055143A1):**

Applicant argued, "Saito relates to an apatite-coated solid composition. Preformed apatite particles and a medicinal are simply mixed with a polyester. It does not relate to a composition where the active agents are "dispersed throughout *a matrix"* having a coating and wherein the

matrix is "the *hydration reaction product of an aqueous mixture comprised of: an inorganic compound capable of undergoing hydration and/or crystallization,* a matrix polymer, wherein said inorganic compound of said matrix becomes a solid by hydration and/or crystallization."

Bell relates to a bone precursor composition comprising a calcium cement which is suitable for injection, wherein said calcium cement includes monobasic calcium phosphate monohydrate and beta-tricalcium phosphate. However as noted above, the "coated solid compositions" of Saito are very different from the matrix composition of the subject invention and combining Saito and Bell would in no way arrive at the composition of the subject invention. There is no suggestion in these references of a sustained release matrix having a coating. In direct contrast, the subject drug delivery matrix according to the present invention is coated after manufacture in order to manipulate the release profile."

Applicant's arguments have been fully considered but they are not persuasive. Applicant's arguments are directed to the manner by which their composition is formed, such as by the 'dispersion of a drug throughout a matrix wherein the matrix is coated and being the hydration reaction product of an aqueous mixture of: an inorganic compound (capable of undergoing hydration and/or crystallization) and a matrix polymer, said inorganic compound becoming a solid by hydration and/or crystallization'. It is the position of the Examiner that the teachings of the prior art are sufficient to render the instant claims *prima facie* obvious. The prior art teaches a controlled release composition comprising the same components as claimed by Applicant. Namely, the prior art in combination recognizes and teaches compositions containing an apatite-coated solid composition containing a matrix polymer and a medicinal substance (i.e., anti–tumor agents such as antineoplastics), whereby the composition has

sustained release properties. A method for producing the solid composition is also disclosed (see column 1, lines 6-10); (col. 2, line 39 – col. 3, line 37). The composition further teaches matrix polymers such as the polysaccharide - hyaluronic acid (col. 20, lines 9-32) and inorganic compounds capable of undergoing hydration and/or crystallization, such as calcium sulfate hemihydrate (col. 15, lines 21-33). Thus, the process by which the instant composition is formed does not impart patentability to the claims. Applicant's argument that the "subject drug delivery matrix according to the present invention is coated after manufacture in order to manipulate the release profile" was not persuasive. The reference of Saito teaches coated compositions. Moreover, the Examiner notes that there are no dissolution or release profiles claimed that would distinguish over the coated compositions of the art; the art being clearly suggestive of a controlled release composition formed of the same elements as desired by Applicant. "[E]ven though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." In re Thorpe, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985).

In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir.

1992). In this case, it is noted that while Saito does not teach the matrix polymer – dextran sulfate, the secondary reference of Bell remedies this deficiency of Saito. Bell teaches that it is well known to one of ordinary skill in the art to employ matrix polymers, such as the polysaccharide dextran sulfate in bone compositions. Note that Bell also teaches inorganic compounds capable of undergoing hydration and/or crystallization, such as calcium sulfate hemihydrate. Additional agents disclosed by Bell include matrix polymer such as chondroitin sulfate and hyaluronic acid [0072-0073]. Thus, both references are drawn to the same field of use (bone forming/precursor compositions). One would incorporate the matrix polymer dextran sulfate, as taught by Bell within the bone compositions of Saito, since the use of these matrix polymers in bone compositions is routine to one skilled in the art. Absent a showing of evidence to the contrary, the formulations of the prior art would achieve the same beneficial results as instantly sought by Applicant.

- **Rejection under 35 U.S.C. §103(a) over Saito (USPN 6,344,209) & Bell (US 2002/0055143A1) in view of Petersen (US 2002/0071827):**

Applicant argued, "The Examiner asserts that it would have been obvious to one of ordinary skill in the art at the time the invention was made to incorporate the HPMC of Petersen within the apatite-coated composition of Saito. However as noted above, the "coated solid composition" of Saito is very different from the matrix composition of the subject invention and combining Saito, Bell and Petersen would in no way arrive at the composition of claim 18."

Applicant's arguments were not rendered persuasive. As delineated above, Applicant's arguments are directed to the manner by which their composition is formed, such as by the dispersion of a drug throughout a matrix wherein the matrix is coated and being the hydration reaction product of an aqueous mixture of: an inorganic compound (capable of undergoing hydration and/or crystallization) and a matrix polymer, said inorganic compound becoming a solid by hydration and/or crystallization. It is the position of the Examiner that the teachings of the prior art are sufficient to render the instant claims *prima facie* obvious. The prior art, in combination, teaches a controlled release composition comprising the same components as claimed by Applicant. Thus, the process by which the instant composition is formed (i.e., hydration reaction) does not impart and accord patentability to the claims. It is noted that Saito's compositions are coated but they do not teach a coating of HPMC (hydroxypropylmethyl cellulose). Petersen is relied upon for the teaching of the use of HPMC in bone graft substitute compositions. Regarding the instant coating, there are no dissolution or release profiles claimed that would distinguish over the coated compositions of the art; the art is clearly suggestive of a controlled release composition formed of these same elements as desired by Applicant. Where the claimed and prior art products are identical or substantially identical in structure or composition, or are produced by identical or substantially identical processes, a prima facie case of either anticipation or obviousness has been established. *In re Best*, 562 F.2d 1252, 1255, 195 USPQ 430, 433 (CCPA 1977). Furthermore, "When the PTO shows a sound basis for believing that the products of the applicant and the prior art are the same, the applicant has the burden of showing that they are not." *In re Spada*, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). Absent a showing of evidence to the contrary, the formulations of the prior art would

achieve the same beneficial results as instantly sought by Applicant; the process by which the product is made failing to accord patentable weight to the present claims.

- **Rejection under 35 U.S.C. §103(a) over Petersen (US 2002/0071827) in view of Bell (US 2002/0055143A1):**

Applicant argued, "The Examiner asserts that it would have been obvious to one of ordinary skill in the art at the time the invention was made to incorporate the glucosaminoglycans and polysaccharides of Bell within the bone graft substitute compositions of Petersen. There is no discussion in these references alone or in combination of a sustained release matrix having a coating.

Applicant's arguments were rendered persuasive. Accordingly, this rejection has been withdrawn.

- **Double Patenting:**

Applicant argued, "None of the commonly owned cases relate to a matrix having a coating. Nor is there any reference of such a matrix with a coating. As such, the commonly owned cases are not obvious variants of the present invention."

Applicant's arguments have been considered but were not rendered persuasive. Each of the Patents cited ((1) 6,869,976 Patent; 6,391,336 Patent; 6,497,901 Patent)) and the copending Application (No. 10/838,303) claim a solid composition and/or method of treatment and/or matrix delivery system formed by a hydration reaction comprising an inorganic compound (calcium sulfate hemihydrate); an active agent, a matrix polymer and/or complexing agent; the only distinction being the coating of the present invention, which would be an obvious variant in

controlled release compositions. Accordingly, the double patenting rejections have been maintained.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

--No claims are allowed at this time.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Humera N. Sheikh whose telephone number is (571) 272-0604. The examiner can normally be reached on Monday-Friday during regular business hours.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward, can be reached on (571) 272-8373. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have any questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Humera N. Sheikh/

Primary Examiner, Art Unit 1615

hns

June 25, 2009